U.S. Serial No.: 10/518,003

Filed: December 10, 2004

Page: 3

Amendments to the Claims:

1. (Canceled)

pharmaceutical composition 2. (Currently amended) Α comprising a[[n]] pharmaceutically effective amount of a combination of ATP-depleting agents at concentrations which deplete in combination with a pharmaceutically acceptable carrier, wherein the ATP-depleting agents synergistically deplete the ATP level of cancer cells to at least 15% or less of normal in cancer cells, and wherein at least one of the ATP-depleting agents is a mitochondrial ATP-inhibitor, a glycolytic inhibitor, a methylthioadenosine phosphorylase inhibitor inhibitor of [[D]]de [[N]]novo purine synthesis with the proviso that other than 6-Methylmercaptopurine 6methylmercaptopurine riboside is not one of said inhibitors.

- 3. (Currently amended) The composition of claim 2, wherein said composition produces a substantially better effect than a composition without at least one of the following ATP-depleting agents a mitochondrial ATPinhibitor, glycolytic inhibitor, a а methylthioadenosine phosphorylase inhibitor or inhibitor of [[D]]de [[N]]novo purine synthesis with the proviso that other than 6 Methylmercaptopurine 6methylmercaptopurine riboside is not one of said inhibitors.
- 4. (Previously presented) The composition of claim 2, further comprising a pyrimidine-depleting agent or a pyrimidine antagonist.
- 5. (Previously presented) The composition of claim 2,

Applicants : MARTIN, et al. U.S. Serial No.: 10/518,003

Filed: December 10, 2004

Page: 4

further comprising an anticancer agent.

- 6. (Original) The composition of claim 5, wherein the anticancer agent to which the cancer is sensitive.
- 7. (Currently amended) The composition of claim 5, wherein the anticancer agent is <u>administered</u> at approximately half of the maximum tolerated dose.
- 8. (Currently amended) The composition of claim 2, wherein the ATP-depleting agents——is comprise 6-methylmercaptopurine riboside (MMPR), 6-Aminonicotinamide (6-AN), alanosine (AL) or a combination thereof.
- 9. (Original) The composition of claim 8, further comprising N-(phosphonacetyl)-L-aspartic acid (PALA).
- 10. (Original) The composition of claim 9, further comprising 3-bromopyruvic acid.
- 12. (Original) The composition of claim 11, further comprising N-(phosphonacetyl)-L-aspartic acid (PALA).
- 13. (Original) The composition of claim 11, further comprising dehydroepiandrosterone (DHEA).
- 14. (Original) The composition of claim 11, further comprising oxythiamine (OT).
- 15. (Original) The composition of claim 11, further

U.S. Serial No.: 10/518,003

Filed: December 10, 2004

Page : 5

comprising dehydroepiandrosterone (DHEA) and oxythiamine (OT).

- 16. (Original) The composition of claim 11, further comprising 6-Aminonicotinomide (6-AN).
- 17. (Canceled)
- 18. (Canceled)
- 19. (Canceled)
- 20. (Canceled)
- (Currently amended) A method for treating a cancer 21. subject comprising administering to the subject a combination of ATP-depleting agents at concentrations which deplete the ATP level to at least 15% of normal in cancer cells wherein at least one of the ATPdepleting agents is a mitochondrial ATP-inhibitor, a inhibitor, methylthioadenosine glycolytic a phosphorylase inhibitor or an inhibitor of [[D]]de [[N]] novo purine synthesis with the proviso that other than 6-Methylmercaptopurine 6-methylmercaptopurine riboside is not one of said inhibitors, wherein said composition produces a substantially better effect than a composition without at least one of the following ATP-depleting agents: a mitochondrial ATP-inhibitor, a inhibitor, a methylthioadenosine glycolytic phosphorylase inhibitor or an inhibitor of [[D]]de [[N]] novo purine synthesis with the proviso that other 6-methylmercaptopurine than - 6-Methylmercaptopurine riboside is not one of said inhibitors.

U.S. Serial No.: 10/518,003
Filed : December 10

December 10, 2004 Filed :

Page :

(Original) A method for treating drug-resistant cancer 46. cells comprising contacting the said cancer with a combination of ATP-depleting agents and an anticancer agent.

- (Original) The method of claim 46, wherein the dose of 47. said anticancer agent is at approximately half of the maximal tolerated dose.
- (Currently amended) The method of claim 46, wherein the 48. ATP level is depleted to at least 15% of normal in cancer cells and at least one of the ATP-depleting agents is a mitochondrial ATP-inhibitor, a glycolytic methylthioadenosine phosphorylase inhibitor, a inhibitor or an inhibitor of [[D]]de [[N]]novo purine synthesis with the proviso that other than 6 Methylmercaptopurine 6-methylmercaptopurine riboside is not one of said inhibitors.
- 49. (Currently amended) The method of claim 46, wherein the ATP level is depleted to at least 15% of normal in cancer cells and at least one of the ATP-depleting agents is a mitochondrial ATP-inhibitor, a glycolytic inhibitor, a methylthioadenosine phosphorylase inhibitor or an inhibitor of [[D]]de [[N]]novo purine synthesis with the proviso that other—than—6— Methylmercaptopurine 6-methylmercaptopurine riboside is not one of said inhibitors and said composition substantially better effect than produces a composition without at least one of the ATP-depleting agents: a mitochondrial ATP-inhibitor, a glycolytic methylthioadenosine phosphorylase inhibitor, a inhibitor and an inhibitor of [[D]]de [[N]]novo purine

U.S. Serial No.: 10/518,003

Filed: December 10, 2004

Page: 7

synthesis with the proviso that other than 6-Methylmercaptopurine 6-methylmercaptopurine riboside is not one of said inhibitors.

50-53. (Canceled)

- 54. (New) A composition comprising an effective amount of a combination of ATP-depleting agents at concentrations which deplete the ATP level to 15% or less of normal in cancer cells, wherein the combination comprises 6-methylmercaptopurine riboside (MMPR), 6-Aminonicotinamide (6-AN) and N-(phosphonacetyl)-L-aspartic acid (PALA), and wherein the cancer cells are breast, ovarian or pancreatic cancer cells.
- 55. (New) A composition comprising an effective amount of a combination of ATP-depleting agents at concentrations which deplete the ATP level to 15% or less of normal in cancer cells, wherein the combination comprises N-(phosphonacetyl)-L-aspartic acid (PALA), alanosine (AL), and 6-methylmercaptopurine riboside (MMPR), and wherein the cancer cells are breast, ovarian or pancreatic cancer cells.
- 56. (New) The Composition of claim 54, wherein the combination further comprises dehydroepiandrosterone (DHEA) and oxythiamine (OT).
- 57. (New) The Composition of claim 55, wherein the combination further comprises dehydroepiandrosterone (DHEA) and oxythiamine (OT).
- 58. (New) The composition of claim 55, wherein the combination further comprises 3-Bromopyruvate (BrPA).

U.S. Serial No.: 10/518,003

Filed: December 10, 2004

Page: 8

59. (New) The composition of claim 55, wherein the combination further comprises Adria, and wherein the amount of Adria administered is one-half the maximum tolerated dosage.

- 60. (New) The composition of claim 55, wherein the combination further comprises BrPA and Adria, and wherein the amount of Adria administered is one-half the maximum tolerated dosage.
- 61. (New) The composition of claim 55, wherein the combination further comprises F16.
- 62. (New) The composition of claim 54, wherein the combination further comprises F16.
- 63. (New) A method for treating a cancer subject comprising administering to the subject the composition of claim 54, wherein the cancer or breast, ovarian or pancreatic cancer.
- 64. (New) A method for treating a cancer subject comprising administering to the subject the composition of claim 55, wherein the cancer or breast, ovarian or pancreatic cancer.